

Roche's Tecentriq in combination with chemotherapy helped people live significantly longer as an initial treatment for people with extensive-stage small cell lung cancer

- **First Phase III study to show a cancer immunotherapy-based combination significantly improved overall survival (OS) and progression-free survival (PFS) in the initial treatment of extensive-stage small cell lung cancer (ES-SCLC)**
- **Data will be presented at the 2018 World Conference on Lung Cancer (WCLC) Presidential Symposium, featured in the press programme and simultaneously published in the *New England Journal of Medicine* on 25 September 2018**

Basel, 25 September 2018 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the Phase III IMpower133 study of Tecentriq® (atezolizumab) plus carboplatin and etoposide (chemotherapy) for the initial (first-line) treatment of people with previously-untreated extensive-stage small cell lung cancer (ES-SCLC). The analysis showed that Tecentriq and chemotherapy helped people live significantly longer compared with chemotherapy alone (overall survival [OS]=12.3 versus 10.3 months; hazard ratio [HR]=0.70, 95% CI: 0.54-0.91; p=0.0069) in the intention-to-treat (ITT) population. [1] The Tecentriq -based combination also significantly reduced the risk of disease worsening or death (progression-free survival, PFS) compared with chemotherapy alone (PFS=5.2 versus 4.3 months; HR=0.77, 95% CI: 0.62-0.96; p=0.017). [1] Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of the individual medicines, and no new safety signals were identified with the combination.

“The results with this Tecentriq combination in the initial treatment of extensive-stage small cell lung cancer represent the first clinically meaningful advance in the disease in over 20 years,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “Our goal is to find treatment options for all types of lung cancer, and we are eager to work with global health authorities to bring this Tecentriq regimen to people living with this particularly difficult-to-treat form of lung cancer as soon as possible.”

The data will be presented at the International Association for the Study of Lung Cancer (IASLC) 2018 World Conference on Lung Cancer (WCLC) Presidential Symposium on Tuesday, September 25, 2018, 9:00 - 9:15 a.m. EDT (Abstracts PL02.07 Oral). The data will be simultaneously published in the *New England Journal of Medicine*, and will be featured in the WCLC press conference at 09:45-10:30 a.m. EDT.

About the IMpower133 study

IMpower133 is a Phase III, multicentre, double-blinded, randomised placebo-controlled study evaluating the efficacy and safety of Tecentriq in combination with chemotherapy (carboplatin and etoposide) versus chemotherapy (carboplatin plus etoposide) alone in chemotherapy-naïve people with ES-SCLC.

The study enrolled 403 people who were randomised equally (1:1) to receive:

- Tecentriq in combination with carboplatin and etoposide (Arm A), or
- Placebo in combination with carboplatin and etoposide (Arm B, control arm)

During the treatment-induction phase, people received treatment on 21-day cycles for four cycles, followed by maintenance with Tecentriq or placebo until progressive disease (PD) as assessed by the investigator using Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1). Treatment could be continued until persistent radiographic PD or symptomatic deterioration was observed.

The co-primary endpoints were:

- PFS as determined by the investigator using RECIST v1.1 in the ITT population
- OS in the ITT population

IMpower133 met its OS and PFS co-primary endpoints as per the study protocol. A summary of the results is included below:

| Arm A (Tecentriq plus chemotherapy) vs Arm B (Placebo plus chemotherapy) in ITT | | |
|--|------------------------------|------------------------|
| | Arm A n=201 | Arm B n=202 |
| Median OS (95% CI), months | 12.3 (10.8, 15.9) | 10.3 (9.3, 11.3) |
| HR (95% CI); P value | 0.70 (0.54, 0.91); p=0.0069 | |
| 1-year OS rate | 51.7% | 38.2% |
| ORR, % | 60% | 64% |
| Median DOR, months | 4.2 | 3.9 |
| HR (95% CI) | 0.70 (0.53, 0.92) | |
| Median PFS (95% CI), months | 5.2 (4.4, 5.6) | 4.3 (4.2, 4.5) |
| HR (95% CI) | 0.77 (0.62, 0.96) p=0.017 | |
| 1-year PFS rate | 12.6% | 5.4% |
| CI, confidence interval; DOR, duration of response; HR, hazard ratio; ORR, objective response rate; PFS, progression-free survival | | |

Safety for the Tecentriq and chemotherapy combination appeared consistent with the known safety profile of the individual medicines, and no new safety signals were identified with the combination. Grade 3-4 treatment-related adverse events (AEs) were reported in 56.6 percent of people receiving Tecentriq plus chemotherapy compared to 56.1 percent of people receiving chemotherapy alone.

About SCLC

Lung cancer is the leading cause of cancer death globally. ^[2] Each year 1.76 million people die as a result of the disease; this translates into more than 4,800 deaths worldwide every day. ^[2] Lung cancer can be broadly divided into two major types: non-small cell lung cancer (NSCLC) and SCLC, with SCLC accounting for approximately 15% of all lung cancer cases. ^[3] Survival rates for people with SCLC vary depending on the stage (extent) of the cancer at the time of diagnosis. ^[4] The five-year relative survival rate for people with stage I SCLC is approximately 31%; however, at stage IV, the five-year relative survival rate declines to approximately 2%.^[5]

About Tecentriq

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1 expressed on tumour cells and tumour-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, Tecentriq may enable the activation of T cells. Tecentriq has the potential to be used as a foundational combination partner with cancer immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers.

Currently, Roche has eight Phase III lung cancer studies underway, evaluating Tecentriq alone or in combination with other medicines.

Tecentriq is already approved in the European Union, United States and more than 70 countries for people with previously treated metastatic NSCLC and for certain types of untreated or previously treated metastatic urothelial carcinoma (mUC).

About Roche in cancer immunotherapy

For more than 50 years, Roche has been developing medicines with the goal to redefine treatment in oncology. Today, we're investing more than ever in our effort to bring innovative treatment options that help a person's own immune system fight cancer.

By applying our seminal research in immune tumour profiling within the framework of the Roche-devised cancer immunity cycle, we are accelerating and expanding the transformative benefits with Tecentriq to a greater number of people living with cancer. Our cancer immunotherapy development programme takes a comprehensive approach in pursuing the goal of restoring cancer immunity to improve outcomes for patients.

To learn more about the Roche approach to cancer immunotherapy please follow this link:

http://www.roche.com/research_and_development/what_we_are_working_on/oncology/cancer-immunotherapy.htm

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. Thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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References

- [1] Liu S.V et al. IMpower133: Primary PFS, OS and safety in a Ph1/3 study of 1L atezolizumab + carboplatin + etoposide in extensive-stage SCLC. Presented at: International Association for the Study of Lung Cancer's (IASLC) 2018 World Conference on Lung Cancer (WCLC); 2018 Sept 23-26; Toronto, Ont, Canada. Abstract #PL02.07
- [2] World Health Organization. GLOBOCAN 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. [Internet]: <http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>. Accessed September 2018.
- [3] Alvarado-Luna and Morales-Espinosa. Transl Lung Cancer Res 2016.
- [4] American Cancer Society; Key Statistics for Small Cell Lung Cancer [Internet]: <https://www.cancer.org/cancer/small-cell-lung-cancer/about/key-statistics.html>. Accessed September 2018.
- [5] American Cancer Society; Small Cell Lung Cancer Survival Rates, by Stage [Internet]: <https://www.cancer.org/cancer/small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html>. Accessed September 2018.

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